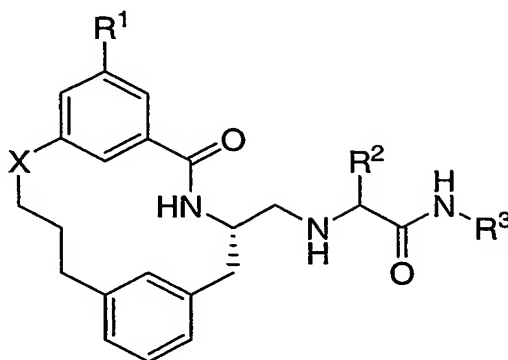


WHAT IS CLAIMED IS:

1. A compound of the formula I:



I

wherein:

R¹ is selected from the group consisting of:

- (1) hydrogen,
- (2) R⁴-S(O)_pN(R⁵)-,

wherein R⁴ is independently selected from the group consisting of:

- (a) -C₁₋₈alkyl, which is unsubstituted or substituted with 1-6 fluoro,
- (b) -NR⁵R⁶,
- (c) phenyl, and
- (d) benzyl,

wherein R⁵ and R⁶ are independently selected from the group consisting of:

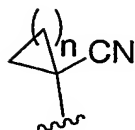
- (a) hydrogen,
- (b) -C₁₋₆alkyl, which is unsubstituted or substituted with 1-6 fluoro,
- (c) phenyl, and
- (d) benzyl,

and wherein p is independently 0, 1, or 2,

- (3) -CN,
- (4) -C₁₋₆alkyl-CN,
- (5) halogen,
- (6) phenyl, which is unsubstituted or substituted with 1-5 substituents where the substituents are independently selected from:

- (a) -CN,
- (b) halo,
- (c) -C₁₋₆alkyl,
- (d) -O-R⁵,
- (e) -CO₂R⁵, and
- (f) -C(O)R⁵,

(7)



wherein n is 1, 2, 3 or 4;

R² is selected from the group consisting of:

- (1) hydrogen,
- (2) -C₁₋₆alkyl, -C₂₋₆alkenyl, -C₂₋₆alkynyl, or -C₃₋₈cycloalkyl which is unsubstituted or substituted with 1-7 substituents where the substituents are independently selected from:
 - (a) halo,
 - (b) hydroxy,
 - (c) -O-C₁₋₆alkyl,
 - (d) -C₃₋₆cycloalkyl,
 - (e) -S(O)_p-C₁₋₆alkyl,
 - (f) -CN,
 - (g) -CO₂H,
 - (h) -CO₂-C₁₋₆alkyl,
 - (i) -CO-NR⁵R⁶,
 - (j) phenyl, which is unsubstituted or substituted with 1-5 substituents where the substituents are independently selected from:
 - (i) -C₁₋₆alkyl,
 - (ii) -CN,
 - (iii) halo,
 - (iv) -CF₃,
 - (v) -O-R⁵, and
 - (vi) -CO₂R⁵,

- (3) phenyl which is unsubstituted or substituted with 1-5 substituents where the substituents are independently selected from:

- (a) -C₁₋₆alkyl,
(b) -CN,
(c) halo,
(d) -CF₃,
(e) -O-R⁵, and
(f) -CO₂R⁵;

- 10 R³ is selected from the group consisting of:

- (1) hydrogen,
(2) -C₁₋₆alkyl, -C₂₋₆alkenyl, -C₂₋₆alkynyl, or -C₃₋₈cycloalkyl which is unsubstituted or substituted with 1-7 substituents where the substituents are independently selected from:

- (a) halo,
(b) hydroxy,
(c) -O-C₁₋₆alkyl,
(d) -C₃₋₆cycloalkyl,
(e) phenyl or pyridyl, which is unsubstituted or substituted with 1-5 substituents where the substituents are independently selected from:

- (i) -C₁₋₆alkyl,
(ii) -CN,
(iii) halo,
(iv) -CF₃,
(v) -O-R⁵, and
(vi) -CO₂R⁵,

- (f) -S(O)_pN(R⁵)-C₁₋₆alkyl, and
(g) -S(O)_pN(R⁵)- phenyl,

- (3) phenyl which is unsubstituted or substituted with 1-5 substituents where the substituents are independently selected from:

- (a) -C₁₋₆alkyl,
(b) -CN,
(c) halo,
(d) -CF₃,

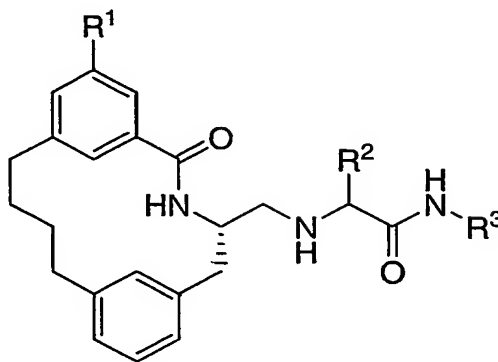
- (e) -O-R⁵, and
 (f) -CO₂R⁵;

X is selected from the group consisting of:

- (1) -CH₂-, and
 (2) -O-;

and pharmaceutically acceptable salts thereof.

2. The compound of Claim 1 of the formula II:



II.

3. The compound of Claim 2 wherein:

R¹ is selected from:

- (1) CH₃-S(O)₂N(CH₃)₂-;
 (2) CH₃CH₂-S(O)₂N(CH₃)₂-;
 (3) (CH₃)₂CH-S(O)₂N(CH₃)₂-;
 (4) phenyl-S(O)₂N(CH₃)₂-; and
 (5) (CH₃)₂N-S(O)₂N(CH₃)₂-;

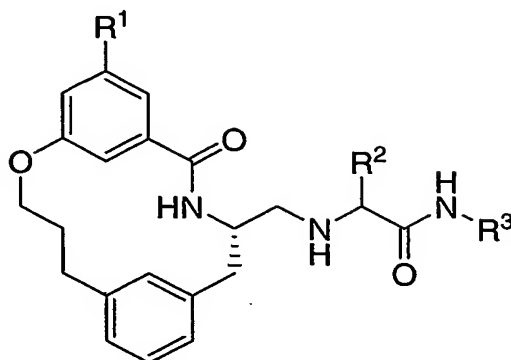
R² is -C₁-6alkyl, unsubstituted or substituted with cyclopropyl or halo;

R³ is -C₁-6alkyl or -C₃-8cycloalkyl; and

X is -CH₂- or -O-;

and pharmaceutically acceptable salts thereof.

4. The compound of Claim 1 of the formula III:



III.

5. The compound of Claim 1 wherein:

R¹ is selected from:

- (1) CH₃-S(O)₂N(CH₃)-;
- (2) CH₃CH₂-S(O)₂N(CH₃)-;
- (3) (CH₃)₂CH-S(O)₂N(CH₃)-;
- (4) phenyl-S(O)₂N(CH₃)-; and
- (5) (CH₃)₂N-S(O)₂N(CH₃)-;

R² is -C₁₋₆alkyl, unsubstituted or substituted with cyclopropyl or halo;

R³ is -C₁₋₆alkyl or -C₃₋₈cycloalkyl; and

X is -CH₂- or -O-;

and pharmaceutically acceptable salts thereof.

6. The compound of Claim 1 wherein:

R¹ is R⁴-S(O)₂N(R⁵)-,

wherein R⁴ is independently selected from the group consisting of:

- (a) -C₁₋₆alkyl, which is unsubstituted or substituted with 1-6 fluoro,
- (b) phenyl, and
- (c) benzyl,

and wherein R⁵ is independently selected from the group consisting of:

- (a) hydrogen,
- (b) -C₁₋₆alkyl, which is unsubstituted or substituted with 1-6 fluoro,

(c) phenyl, and

(d) benzyl.

7. The compound of Claim 6 wherein R^1 is selected from:

- (1) $\text{CH}_3\text{-S(O)}_2\text{N(CH}_3\text{)-}$;
- (2) $\text{CH}_3\text{CH}_2\text{-S(O)}_2\text{N(CH}_3\text{)-}$;
- (3) $(\text{CH}_3)_2\text{CH-S(O)}_2\text{N(CH}_3\text{)-}$; and
- (4) $\text{phenyl-S(O)}_2\text{N(CH}_3\text{)-}$;
- (5) $(\text{CH}_3)_2\text{N-S(O)}_2\text{N(CH}_3\text{)-}$.

8. The compound of Claim 7 wherein R^1 is $\text{CH}_3\text{-S(O)}_2\text{N(CH}_3\text{)-}$.

9. The compound of Claim 1 wherein R^2 is $\text{-C}_1\text{-6alkyl}$, unsubstituted or substituted with cyclopropyl or halo.

10. The compound of Claim 9 wherein R^2 is selected from:

- (1) $\text{CH}_3\text{-}$;
- (2) $\text{CH}_3\text{CH}_2\text{-}$;
- (3) $(\text{CH}_3)_2\text{CH-}$;
- (4) $\text{CH}_3\text{CH}_2\text{CH}_2\text{-}$;
- (5) $(\text{CH}_3)_2\text{CHCH}_2\text{-}$;
- (6) $\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{-}$;
- (7) $\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{-}$;
- (8) $\text{cyclopropyl-CH}_2\text{-}$;
- (9) $\text{CF}_3\text{CH}_2\text{-}$; and
- (10) $\text{CH}_2\text{FCH}_2\text{-}$.

11. The compound of Claim 1 wherein R^3 is $\text{-C}_1\text{-6alkyl}$ or $\text{-C}_3\text{-8cycloalkyl}$.

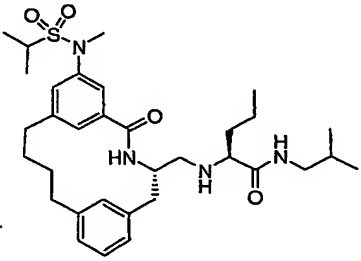
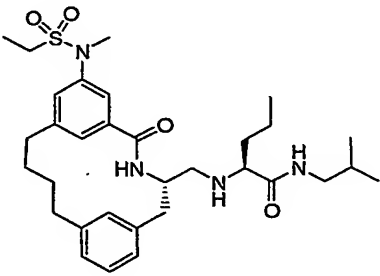
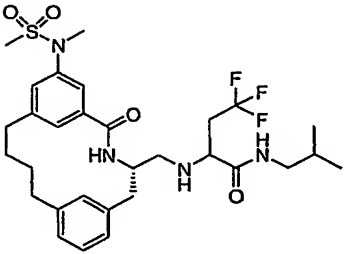
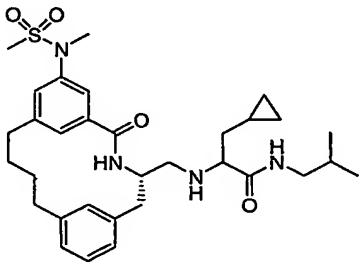
12. The compound of Claim 11 wherein R^3 is selected from:

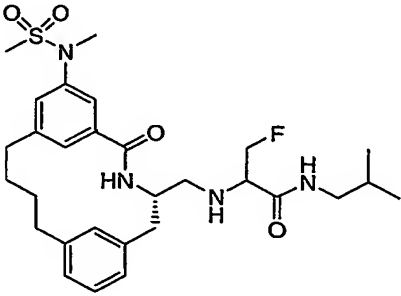
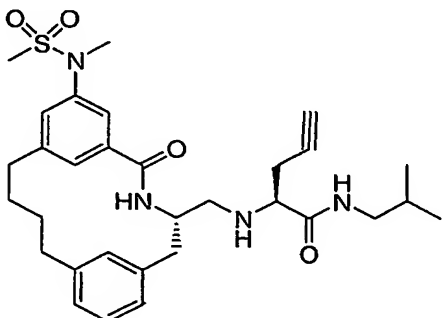
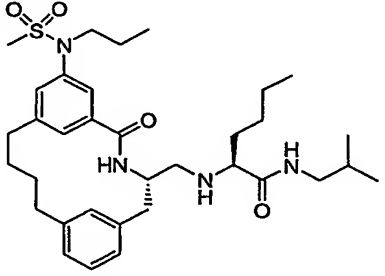
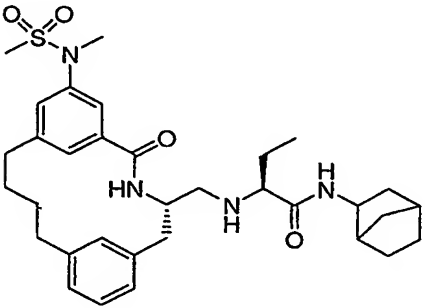
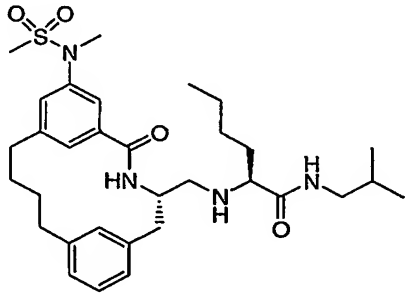
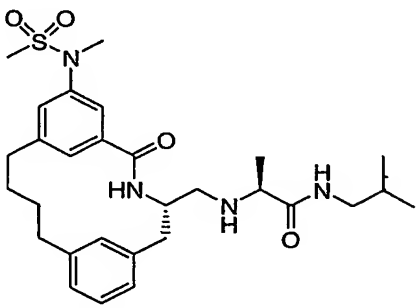
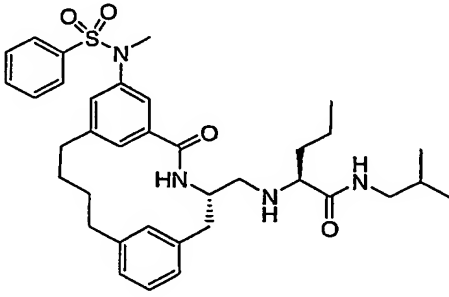
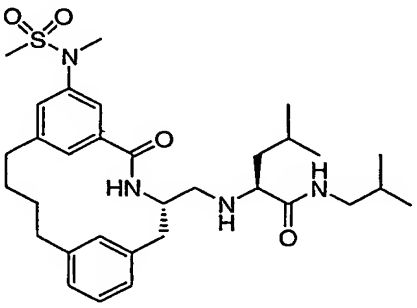
- (1) $\text{CH}_3\text{-}$;
- (2) $\text{CH}_3\text{CH}_2\text{-}$;
- (3) $(\text{CH}_3)_2\text{CH-}$;

- (4) $\text{CH}_3\text{CH}_2\text{CH}_2-$;
 (5) $(\text{CH}_3)_2\text{CHCH}_2-$;
 (6) $\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2-$;
 (7) $\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2-$; and
 (8) bicyclo[2.2.1]heptyl-.

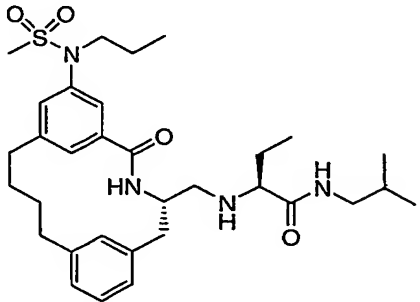
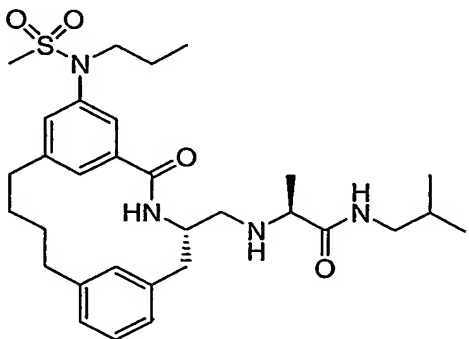
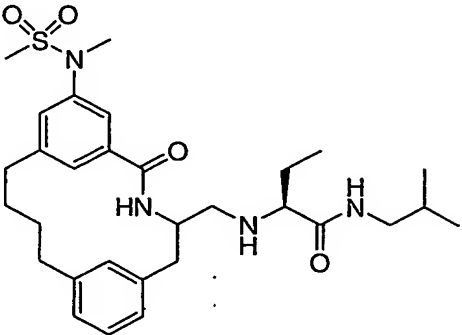
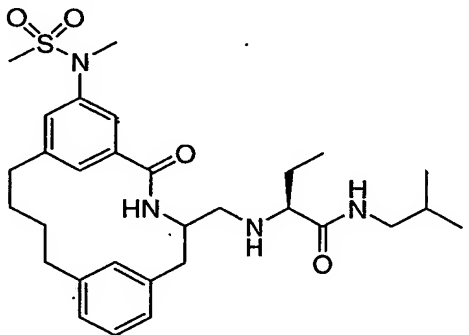
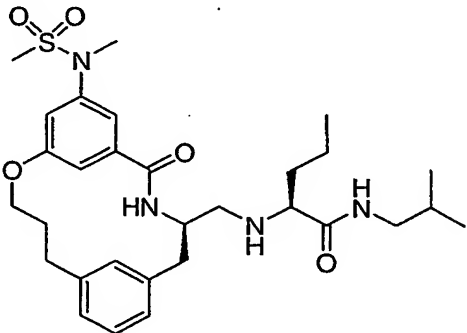
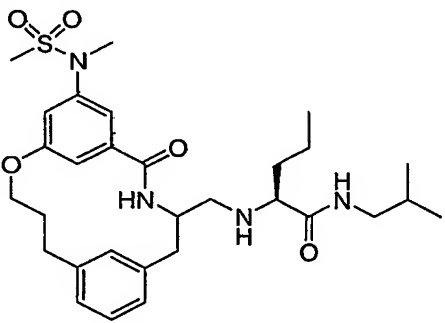
13. The compound of Claim 12 wherein R^3 is $(\text{CH}_3)_2\text{CHCH}_2-$.

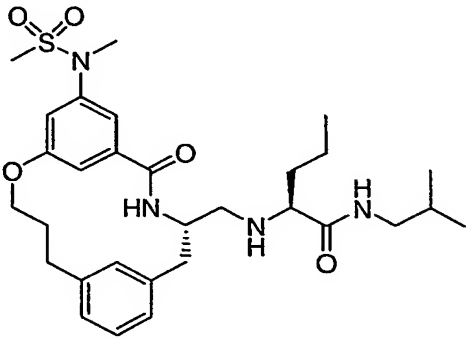
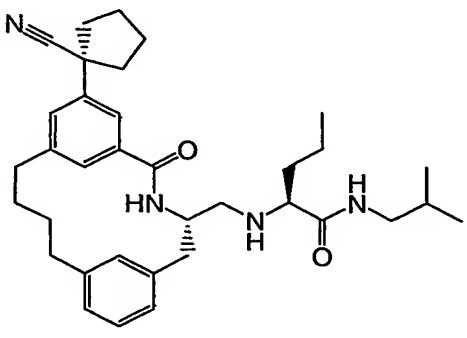
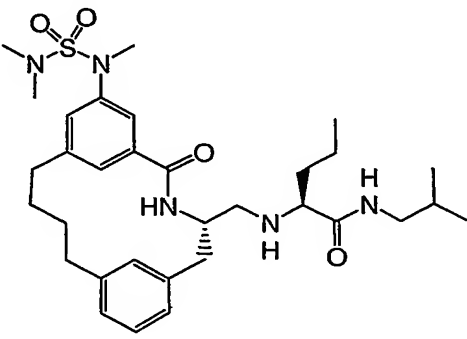
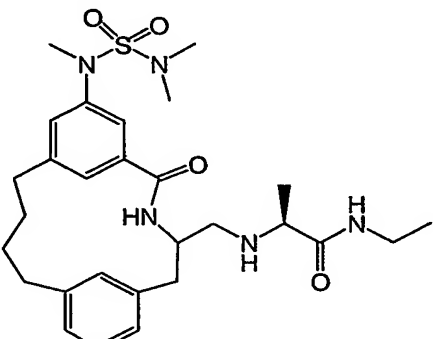
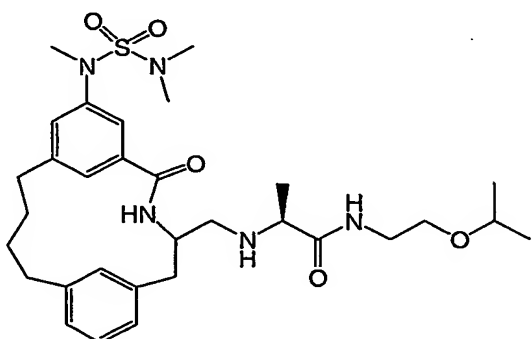
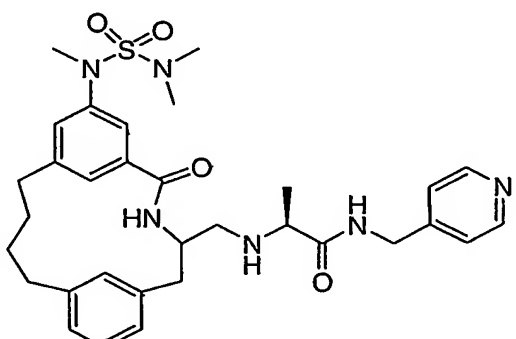
14. A compound which is selected from the group consisting of:

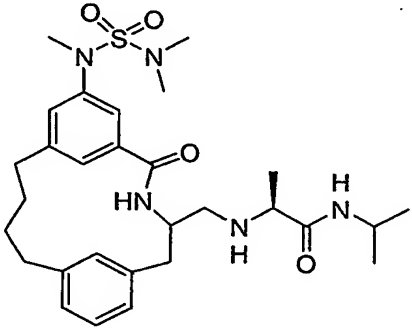
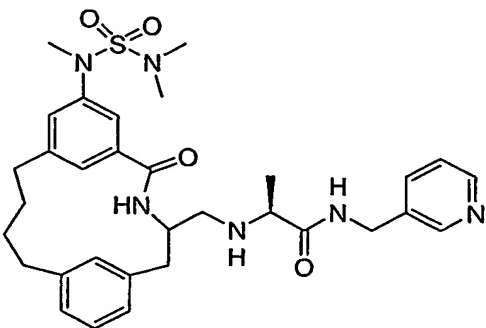
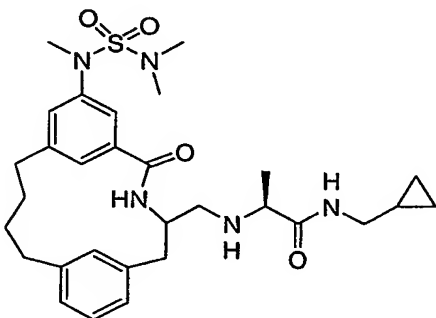
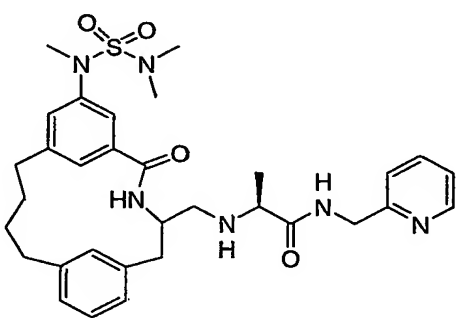
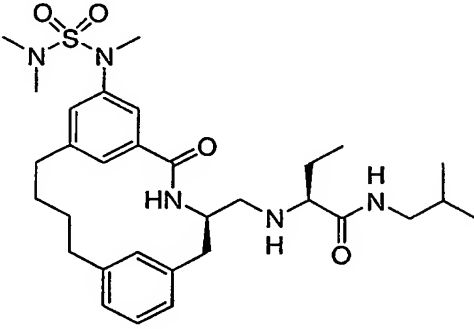
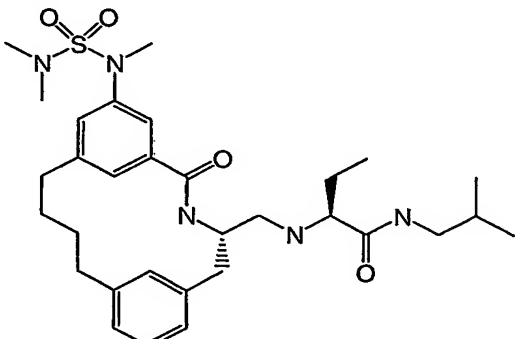
Ex	Structure	Ex	Structure
2		3	
4		5	

Ex	Structure	Ex	Structure
6		7	
8		9	
10		11	
12		13	

Ex	Structure	Ex	Structure
14	 Detailed description: The molecule consists of a 16-membered macrocycle. One part of the ring contains a benzene ring substituted at the para position with a dimethylsulfonyl group (-SO ₂ N(CH ₃) ₂). Another part of the ring contains another benzene ring. The two benzene rings are connected by a -CH ₂ -CH ₂ - linker. Between the two benzene rings, there is an amide bond (-NH-CO-) where the nitrogen is attached to the first benzene ring and the carbonyl carbon is attached to the second benzene ring via a methylene group. Extending from the nitrogen of this amide is a side chain: -CH ₂ -CH ₂ -NH-CH(CH ₃)-C(=O)-NH-CH ₂ -CH(CH ₃) ₂ . Stereochemistry: The methylene group between the two benzylic positions has a dashed bond, indicating it points away from the viewer.	15	 Detailed description: This structure is identical to structure 14 except for the terminal substituent on the side chain. Instead of an isopropylamino group, it features a 1-amino-2-methylpropanoate derivative, specifically -C(=O)-NH-CH(CH ₃)-CH ₂ -NH ₂ .
16	 Detailed description: This structure is identical to structure 14 except for the terminal substituent on the side chain. It features a more complex side chain ending in a carboxylic acid derivative: -C(=O)-NH-CH(CH ₃)-CH ₂ -COOH.	17	 Detailed description: This structure is identical to structure 14 except for the terminal substituent on the side chain. It features a bicyclic amine derivative as the terminal group.
18	 Detailed description: This structure is identical to structure 14 except for the terminal substituent on the side chain. It features a branched alkylamino group as the terminal substituent.	19	 Detailed description: This structure is identical to structure 14 except for the terminal substituent on the side chain. It features a different branched alkylamino group as the terminal substituent.

Ex	Structure	Ex	Structure
20		21	
22		23	
24		25	

Ex	Structure	Ex	Structure
26		27	
28		29	
30		31	

Ex	Structure	Ex	Structure
32		33	
34		35	
36		37	

and pharmaceutically acceptable salts thereof.

15. A pharmaceutical composition comprising an effective amount of a compound of
 5 Claim 1 and a pharmaceutically acceptable carrier.

16. A method for inhibition of β -secretase activity in a mammal in need thereof which comprises administering to the mammal a therapeutically effective amount of a compound of Claim 1.

5 17. A method for treating Alzheimer's disease in a patient in need thereof comprising administering to the patient an effective amount of a compound of Claim 1.